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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/019,214 | 01/10/2003 | Susan M. Logan | 14096.24USWO | 1851 |
| 23552 | 7590 | 02/22/2005 | EXAMINER | |
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| | | | ART UNIT | PAPER NUMBER |
| | | | 1652 | |

DATE MAILED: 02/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

| | | |
|---------------------|--------------|--|
| Application No. | Applicant(s) | |
| 10/019,214 | LOGAN ET AL. | |
| Examiner | Art Unit | |
| Kagnew H Gebreyesus | 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 18 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 59,60,62 and 71 is/are pending in the application.
- 4a) Of the above claim(s) 63-66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Claims 1-58, 61 and 67-70 have been cancelled. Claim 59, 60 and 62-66 and 71 are pending in this application. Claims 59-60, 62 and 71 are now under consideration. Claims 63-66 remain withdrawn from consideration as being drawn to non-elected subject matter.

Applicant's election with traverse of Group IX in the reply filed on January 18, 2005 is acknowledged. The amendment filed on January 18, 2005 under 37 CFR 1.312 has been entered. Applicants traverse the restriction by arguing that in *In Weber and In re Haas* it is stated that restrict within a claim is improper. However it is noted that in these cases restriction within a claim is only improper if the subject matter has unity of invention. Broadly, unity of invention exists where compounds (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility. Given that this restriction is between different enzymes with different sequences the criteria of *Weber and Haas* (i.e. unity of invention) is not met. While the various enzymes may share an overall common utility for LPS biosynthesis, they do not share any structural features disclosed as essential to the shared utility by virtue of their different sequences. In addition applicants suggest that there is no burden in searching claims in Group XIII-XVI, together with group IX. While the search for a mutant *H. pylori* beta-1, 4-galactosyltransferase (HP0826) involved in the biosynthesis of LPS and the search for a vaccine formulation that utilizes the specific enzymes may overlap however each group necessarily requires an independent search and thus the search for each group is not necessarily co-extensive as the applicant suggested. Furthermore since applicants have cancelled claims 1-58, 61 and 67-70 argument traversing restriction is moot. Therefore the requirement for restriction is made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 62 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The scope of the term "open reading frame 0826" is unclear. The specification discloses HP0826 from *H. pylori* strain 26695 and strain *H. pylori* strain SS0826 which correspond to SEQ ID NO 1 and SEQ ID NO: 9 respectively. Does this term refer to a specific sequence, to a specific genetic locus of any *H. pylori* strain or to some other genus of sequences? Furthermore it is also not clear whether the open reading frame refers to *H. pylori* HP0826 from strain 26695 or from strain SS0826 from strain SS1. Applicant's specification does not clearly define the scope of this term and thus the claim is indefinite. For purposes of examination this phrase is taken to be the sequence of a beta-1, 4-galactosyltransferase isolated from *H. pylori* strain 2665 (HP0826) and strain SS1 (SS0826).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 71 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants are claiming a single mutant strain that comprises said LPS structure. However figure 3 clearly distinguishes the LPS structure exhibited by two different strains. Therefore applicants have no support for a single strain which exhibits the LPS depicted in claim 71.

5. Claims 59, 60, 62 and 71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of mutant *H. pylori* deficient in a genus of glycosyltransferases. The construction of such mutant *H. pylori* strain requires an artisan to have possession of the specific gene to be deactivated. The specification teaches the structure of two strains from only one representative species of such glycosyltransferases genes from *H. pylori*. Moreover, the specification fails to describe any other representative species of a mutant glycosyltransferases from *H. pylori* by any identifying characteristics or properties other than the functionality of being a glycosyltransferase. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 59 and 60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 59 and 60 are rejected because the specification, while being enabling for a mutant strain of *H. pylori* having a deactivated beta-1, 4-galactosyltransferase (HP0826) in *Helicobacter pylori* strain 2665 and strain SS1, does not reasonably provide enablement for mutant for any glycosyltransferase enzyme from any strain of *H. pylori*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 59 and 60 are so broad as to encompass any *H. pylori* strain containing mutant glycosyltransferase enzyme encompassing a mutant glucosyltransferase, or a mutant galactosyltransferase or a mutant heptasyltransferase, fucosyltransferase etc. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the large number of glycosyltransferases and diverse strains of *H. pylori* broadly encompassed by the claims. Since glycosyltransferases involved in LPS biosynthesis determine LPS structural and functional properties, predictability of a *H. pylori* strain derived from mutations on these glycosyltransferases singularly or in combination can result in obtaining the desired LPS structure requires a knowledge of and guidance with regard to the type(s) of glycosyltransferase(s), if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the glycosyltransferases mutation relates to the LPS structure. However, in this case the disclosure

is limited to an *H. pylori* (HP0826) beta-1, 4-galactosyltransferase mutant strains derived from wild type strain 2665 and strain SS1.

While recombinant and mutagenesis techniques of single genes are known in for making a specific bacterial strain, it is not routine in the art to perform multiple types of enzyme modifications, as encompassed by the instant claims (glycosyltransferase), with a reasonable expectation of success in obtaining a specific LPS structure and the result of such modifications are unpredictable. In addition, one skilled in the art would expect modification of specific glycosyltransferases alone or in combination would result in LPS structures with corresponding epitopes.

The specification does not support the broad scope of the claims which encompass all mutant strains resulting from deactivation of any glycosyltransferases alone or in combination because the specification does not establish: (A) the specific glycosyltransferase that results in a mutant *H. pylori* strain; (B) the result of deactivating any glycosyltransferase; (C) a rational and predictable scheme for modifying any glycosyltransferase with an expectation of obtaining the desired claimed mutant *H. pylori* strains; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any mutant *H. pylori* strain comprising any number of mutant glycosyltransferases alone or in combination. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired mutant *H. pylori* is unpredictable and

the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claims 59 and 60 are rejected under 35 U.S.C. 102(a) as being anticipated by Appelmek et al. This rejection is based upon the public availability of a printed publication. Claims 59 and 60 are broadly drawn to a mutant strain of *H. pylori*, said mutant strain having deactivated at least one gene encoding any glycosyltransferase involved in the biosynthesis of an *H. pylori* LPS. Appelmek et al. disclose an alpha-3-fucosyltransferase knockout mutant strains of *H. pylori* (which is a glycosyltransferase as broadly interpreted) and confirmed the role of this glycosyltransferase in determining the structure and the mechanism underlying LPS diversity in *H. pylori*. The broad interpretation of claims 59 and 60 encompass, glucosyltransferases, galactosyltransferases, fucosyltransferases, heptosyltransferases etc. Therefor the disclosure by Appelmek et al. clearly anticipates claims 59 and 60 when given the broadest interpretation of these claims.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

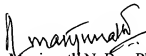
11. Claims 59, 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al., As stated above claims 59 and 60 are broadly drawn to a mutant strain of *H. pylori*, said mutant strain having deactivated at least one gene encoding any glycosyltransferase involved in the biosynthesis of an *H. pylori* LPS. Wang et al. disclose the cloning and characterization of a gene encoding *H. pylori* alpha-1, 2-fucosyltransferase from various *H. pylori* strains and the construction of alpha-1, 2-fucosyltransferase gene knockout mutant strains of *H. pylori* (strain 26695 and UA802) by inserting a CAT cassette at the specific location of the alpha-1, 2- fucosyltransferase gene that led to the loss of Lewis Y (which constitutes part of the LPS O-antigen) production in these mutants. Given that Lewis Y is an integral part of the LPS and that Wang et al., show that the knock-out mutants lost Lewis Y production as shown by ELISA assay and immunoelectron microscopy it clearly teaches the involvement of this particular glycosyltransferase (alpha-1, 2- fucosyltransferases) in the biosynthesis of *H. pylori* LPS . Hence claims 59 and 60 are clearly anticipated by Wang et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30am-5: 30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy ponnathapura can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kagnew Gebreyesus PhD.



Manjunath N. Rao Ph.D
Primary Examiner, Art unit 1652
February, 16, 2005.